



Combination of AsiDNA and PARP Inhibitors Demonstrates Synergistic Effect, Bypasses Genetic Restriction

Preclinical Research Published in Clinical Cancer Research

Paris (France), Copenhagen (Denmark), September 7, 2016 – Onxeo S.A. (Euronext Paris, Nasdaq Copenhagen: ONXEO), an innovative company specialized in the development of orphan oncology therapeutics, today announced results from a preclinical study demonstrating that the synergistic effect of its lead signal-interfering DNA product candidate AsiDNA™ in combination with various products in the PARP (PolyADP-Ribose Polymerase) inhibitor class of drugs is able to bypass the genetic restriction of PARP inhibitors.

The results, which establish potential for rapid clinical translation, were recently published online in the article [“Drug Driven Synthetic Lethality: bypassing tumor cell genetics with a combination of Dbait and PARP inhibitors”](#) in the peer-reviewed journal *Clinical Cancer Research*. The print issue is expected to be published in the coming weeks.

The preclinical study characterized the DNA repair inhibition activity of AsiDNA and olaparib – by monitoring DNA repair and DNA damage, and analyzed cell survival to standalone and combined treatments of 21 different tumor cell lines, including 12 breast cancer cell lines, and 3 non-tumor cells.

Olaparib is a PARP inhibitor, blocking the enzyme PARP involved in tumor DNA repair, with efficacy validated in patients with BRCA gene mutation, leading to accumulation of DNA double-strand breaks which cannot be repaired. Olaparib is approved for women with BRCA-mutated advanced ovarian cancer.

Results showed that olaparib and AsiDNA prevent recruitment of different targeted repair enzymes to damaged sites, and the combination of both drugs increases the accumulation of unrepaired damage, resulting in a synergistic increase of cell death in all tumor cells. Synergistic efficacy of the combination treatment was observed in all tested tumor models regardless of BRCA status, while no increase of DNA damage, nor lethality was observed in healthy cells, suggesting a good safety and tolerability profile. Analysis also demonstrated different molecular mechanisms underlying the response to AsiDNA and olaparib, suggesting that drug resistance to the combination would be a very rare event. Furthermore, the study also showed that the combination with AsiDNA is effective using six different PARP inhibitors, with no toxicity in non-tumor cells.

Graham Dixon, PhD, Chief Scientific Officer of Onxeo, commented, *“PARP inhibitors show significant benefit in cancer patients, but are mostly limited to tumors with BRCA mutations. AsiDNA breaks the cycle of tumor DNA repair by interfering upstream of the DNA repair process, thereby blocking multiple repair pathways and preventing repair regardless of genetic mutation. Combining AsiDNA with already well-researched and FDA-approved PARP inhibitors like olaparib presents a novel, clinically-viable*

strategy with broad applicability. These preclinical results support Onxeo's strategic assessment and advancement plan for AsiDNA, and bolster our options for continued clinical development of AsiDNA as a monotherapy and in combination with anti-cancer agents."

About AsiDNA

AsiDNA is a signal interfering DNA repair pathway inhibitor being developed by Onxeo as an anti-cancer agent. As a short double-stranded DNA molecule, AsiDNA utilizes a unique mechanism of action to break the cycle of tumor DNA repair by interfering at the core of DNA damage, blocking multiple repair pathways, while sparing healthy cells. A first-in-human Phase I clinical trial evaluating AsiDNA in combination with radiotherapy for treatment of patients with metastatic melanoma showed AsiDNA is well tolerated and demonstrated proof of efficacy, with an objective response rate of 59% and a complete response rate of 30% compared to 10% CR with radiotherapy alone. Onxeo is currently accelerating a comprehensive advancement plan for AsiDNA as monotherapy and in combination with anti-cancer agents to offer potential new treatment options for patients suffering from various types of cancer.

About Onxeo

Onxeo is a leading developer of orphan oncology drugs. The Company is focused on developing innovative therapeutics for rare cancers, one of the fastest growing markets in the healthcare industry with high, unmet medical needs. Onxeo's vision is to become a global leader and pioneer in oncology, with a focus on orphan or rare cancers, by developing advanced, effective, and safe therapeutics designed to improve the lives of patients. Onxeo's comprehensive portfolio features a broad orphan oncology pipeline, with four independent programs in various stages of clinical development, including Onxeo's first approved orphan oncology drug, Beleodaq®. The Company is headquartered in Paris, France and has approximately 50 employees. Onxeo is listed on Euronext in Paris, France (Ticker: ONXEO, ISIN Code: FR0010095596) and Nasdaq Copenhagen, Denmark (Ticker: ONXEO).

Onxeo's orphan oncology products are:

- **Livatag®** (Doxorubicin Transdrug™): Currently being evaluated in a Phase III trial (ReLive) in patients with hepatocellular carcinoma (primary liver cancer); and in combination with other cancer agents in first-line HCC
- **Beleodaq®** (belinostat): FDA-approved in the US in 2014 under the agency's accelerated approval program as a second-line treatment for patients with peripheral T-cell lymphoma (PTCL) and currently marketed by Onxeo's partner in the US, Spectrum Pharmaceuticals; belinostat in combination with other cancer agents is currently in development in first-line treatment for patients with PTCL (BelCHOP) and in other solid tumors
- **AsiDNA**: The first-in-class siDNA (signal-interfering DNA) which has successfully undergone a proof-of-concept Phase I trial in metastatic melanoma
- **Validive®** (Clonidine Lauriad®): Positive final results from a Phase II trial in head and neck cancer patients with severe oral mucositis

In addition, Onxeo has successfully developed and registered two non-cancer products, which are currently being commercialized in the U.S. and Europe.

Learn more by visiting www.onxeo.com.

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